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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,207	01/04/2005	Tadafumi Tamura	BJS-4093-6	7702

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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
06/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,207	TAMURA ET AL.	
	Examiner	Art Unit	
	SHARON WEN	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,9-11,13-16 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *11 and 13-15* is/are allowed.

6)☒ Claim(s) *1-3, 5-6, 9-10, 16 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments filed 03/23/2009 have been entered.

Claims 4, 7-8, 12 and 17-48 have been canceled.

Claims 1-3, 5-6, 9-11, 13-16 and 49-51 are pending and currently under examination as they read on a method of treating arthritis comprising administering an antibody which specifically binds to FGF-8.

2. This Action will be in response to Applicant's Arguments/Remarks, filed 03/23/2009.

The rejections of record can be found in the previous Office Action.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-3, 5-6, 9-10, 16 and 49-51 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Seddon et al. (U.S. Patent 5,491,220) in view of Hanai et al. (U.S. Patent 5,952,472) and Owen et al. (*Journal of Immunological Methods*, 1994, 168:149-165).

Applicant's arguments, filed 03/23/2009, have been fully considered but have not been found convincing essentially for the reasons of record and reiterated herein for Applicant's convenience. Applicant's arguments and examiner's rebuttal are essentially the same of record as follows.

The instant claims are directed to a method of treating arthritis comprising administering an anti-FGF-8 antibody to inhibit activity of FGF-8, wherein the antibody is a monoclonal, humanized, i.e., human chimeric or human CDR-grafted, or a fragment thereof.

Seddon et al. teach a method of treating arthritis, in particular, rheumatoid arthritis, comprising administering an inhibitor of FGF (see entire document, in particular, see column 12, lines 42-49).

Seddon et al. did not teach using an antibody as the inhibitor of FGF to treat arthritis. However, antibodies to FGF, particularly anti-FGF-8 antibodies, as inhibitors of FGF, were well known in the art at the time of the invention was made as evidenced by Hanai et al. (see entire document).

Hanai et al. taught a monoclonal antibody that recognized SEQ ID NO: 17 wherein said monoclonal antibody neutralized the activity of FGF-8 (see entire document, in particular, see column 2, lines 9-10). In addition, Hanai et al. taught using the anti-FGF-8 monoclonal antibody which is produced from a hybridoma to treat diseases such as cancer where neovascularization plays a dominant role in the pathogenesis (see Background and Summary of the Invention in columns 1-2).

Although Seddon et al. also did not teach FGF-8 as the specific FGF to target for treating arthritis, given the finite known species of FGF, it would have been obvious to one of ordinary skill in the art to target FGF-8.

The rationale to support a conclusion that the claim would have been obvious is that a person of ordinary skill has good reason to pursue the known options (e.g. administration an anti-FGF-8 antibody for therapeutic purposes as taught by Hanai et al.) within his or her technical grasp. This leads to the anticipated success of treating arthritis with inhibitory anti-FGF-8 antibody. It is likely the product not of innovation but of ordinary skill and common sense.

Given the teachings of the two references, it is *prima facie* obvious to one of ordinary skill in the art, at the time of filing of the instant application, to substitute the anti-FGF-8 antibody as taught by Hanai et al. for the antagonist of FGF in the method of treating arthritis as taught by Seddon et al. for the same purpose of treating arthritis.

An ordinary artisan would have been motivated to use the anti-FGF-8 antibody to treat arthritis given the teaching by Seddon et al. stating FGF antagonists "that acts as angiogenesis inhibitor are useful for the treatment of diseases where neovascularization is dominant in the pathology such as…chronic inflammation, rheumatoid arthritis, and the like" (see column 12, lines 42-49) and the teaching by Hanai et al. in the anti-FGF-8 antibody having the neutralization activity specifically against FGF-8 would be effective in treating

cancer wherein neovascularization is dominant in pathology (see column 1, third paragraph).

Even though the combined teachings of Seddon et al. and Hanai et al. were silent on "inhibiting joint destruction", "protecting cartilage", or "inhibiting growth of synovial membrane" (claims 49-51), given that the combined teachings rendered the claimed method of treating arthritis comprising administering an anti-FGF-8 antibody *prima facie* obvious, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. Therefore, one of ordinary skill would recognize that the same method steps comprising administering the anti-FGF-8 antibody would also be able to inhibit joint destruction, protect cartilage or inhibit growth of synovial membrane.

Seddon et al. and Hanai et al. did not teach a humanized, i.e., human chimeric or human CDR-grafted antibody or the antigen binding fragments thereof. However, it is well known in the art, at the time of filing, to humanize antibodies or obtain the antigen-binding fragments thereof for therapeutic purposes in human as demonstrated by Owens et al. (see entire document).

In particular, Owens et al. taught the methods of making human chimeric antibodies and human CDR-grafted antibodies from rodent monoclonal antibodies (see pages150-155). Moreover, Owens et al. taught the construction of antigen-binding fragments, in particular, F(ab')2, Fab, Fv and scFV, which read on a "CDR-containing peptide" (claim 16) (see Owens et al., pages 155-157).

Given the combined teachings of Seddon et al. and Hanai et al., in view of Owens et al., it is prima facie obvious to one of ordinary skill in the art, at the time of filing of the instant application, to substitute the anti-FGF-8 antibody as taught by Hanai et al. for the FGF-8 antisense molecule in the method of treating arthritis as taught be Seddon et al. for the same purpose of treating arthritis, wherein the antibody is human chimeric, human CDR-grafted or antigen-binding fragments thereof as taught by Owens et al.

An ordinary artisan would have been motivated to humanize the antibody according to the methods taught by Owens et al. because Owens et al. teach a need for humanizing rodent monoclonal antibodies due to problems associated with using the rodent monoclonal antibodies in human therapy and advantages associated with using antigen binding fragments thereof, i.e., shorter half-lives in vivo (see Introduction on page 149).

Therefore, the invention, as a whole, was *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

In response to Applicant's argument that Seddon et al. did not teach or suggest FGF-8 as the specific FGF to target for treating arthritis, the following is noted.

Although Seddon et al. did not teach FGF-8 as the specific FGF to target for treating arthritis, given the finite known species of FGF, it would have been obvious to one of ordinary skill in the art to target FGF-8.

The rationale to support a conclusion that the claim would have been obvious is that a person of ordinary skill has good reason to pursue the known options (e.g. administration an anti-FGF-8 antibody for therapeutic purposes as taught by Hanai et al.) within his or her technical grasp. This leads to the anticipated success of treating arthritis with inhibitory anti-FGF-8 antibody. It is likely the product not of innovation but of ordinary skill and common sense.

Given that anti-FGF-8 antibody was a known inhibitor of FGF-8 as taught by Hanai et al., it would have been within the ordinary artisan's technical grasp to use Hanai's the antibody as an inhibitor of FGF-8 to treat arthritis as taught by Seddon et al.

Applicant's arguments have not been persuasive. Therefore this rejection is maintained for reasons of record.

Conclusion

5. Claims 11 and 13-15 are allowed.

Claims 1-3, 5-6, 9-10, 16 and 49-51 are rejected.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Examiner, Art Unit 1644
June 4, 2009

/Phillip Gambel/
Primary Examiner
Technology Center 1600
Art Unit 1644
June 7, 2009